1.0 PURPOSE

The purpose of this policy is to provide guidance in determining whether an Investigational New Drug Application (IND) needs to be filed with the U.S. Food and Drug Administration (FDA).

2.0 SCOPE

This policy applies to all clinical trials funded and/or sponsored by DAIDS. This may include clinical trials evaluating investigational drugs and/or biological products that are lawfully marketed in the United States.

3.0 BACKGROUND

DAIDS collaborates with industry, academia, the international scientific community and the communities of persons most affected by HIV/AIDS to develop and test drugs and biological products to prevent and manage HIV infection. DAIDS complies with all applicable U.S. regulations governing the evaluation of investigational drugs or biological products. The IND is the formal submission made to the FDA that indicates a sponsor's intention to conduct a clinical trial with an investigational drug or biological product. It is the means through which the sponsor technically obtains the authorization to conduct clinical trials according to the protocols approved in the IND application.

4.0 DEFINITIONS

Biological product – means any virus, therapeutic serum, toxin, antitoxin, or analogous product available to prevent, treat or cure diseases or injuries in man. The terms "biological product" or "biologic" are deemed to be synonymous for purposes of this policy.

Clinical investigation – means any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects.

Code of Federal Regulation (CFR) – is the regulatory and legal guide for the preparation of INDs to be submitted to either the Center for Biologics Evaluation and Research (CBER) or the Center for Drug Evaluation and Research (CDER).

Drug – means articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals.

U. S. Food and Drug Administration (FDA) – is a public health agency within the United States Department of Health and Human Services. FDA's mission is to promote and protect public health by helping safe and effective products reach the market in a timely way and monitoring of products for continued safety after they are in use as authorized by The

Federal Food and Cosmetic Act. The Agency regulates all clinical investigations in support of marketing applications.

IND – means an investigational new drug application.

Investigational new drug – means a new drug or biological product that is used in a clinical investigation. The terms "investigational new drug" and "investigational drug" are deemed to be synonymous for purposes of this policy.

Legally marketed product – is a product that received U.S. licensure.

Principle Investigator (PI) – is a qualified person designated by the applicant institution to direct the research. PIs oversee the scientific and technical aspects of a grant and the day-to-day management of the research.

Regulatory Affairs Branch (RAB) – is a branch in the Office for Policy in Clinical Research Operations (OPCRO) in the Division of AIDS (DAIDS). RAB performs regulatory surveillance over all clinical trials sponsored and funded by DAIDS.

Sponsor – means a person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual or pharmaceutical company, government agency, academic institution, private organization, or other organization. The sponsor does not actually conduct the investigation unless the sponsor is a sponsor-investigator. In this policy, DAIDS will be the sponsor for the majority of the INDs.

Sponsor-Investigator – is an individual who both initiates and actually conducts, alone or with others, a clinical investigation, that is, under whose immediate direction the test article is administered, dispensed to, or used involving a subject and who also submitted the IND.

Subject – means a human who participates in an investigation, either as a recipient of the investigational new drug or as a control. A subject may be a healthy human or a patient with a disease.

For additional definitions see DAIDS glossary.

5.0 RESPONSIBILITIES

RAB – is responsible for determining if a clinical trial needs to be conducted under an IND in accordance with the applicable U.S. regulations. This decision may require RAB's consultation with the FDA, pharmaceutical companies, protocol team and/or PI and other DAIDS program staff.

6.0 POLICY

IND Sponsor

DAIDS reserves the right to serve as the IND Sponsor of any clinical trial that it funds. In some circumstances, DAIDS may agree, in advance and through a Clinical Trial Agreement (CTA) that a pharmaceutical company collaborator serves as the Sponsor. On a select, case-by-case basis, DAIDS may agree that an investigator serve as the Sponsor (Sponsor-Investigator). The specific requirements of the Sponsor-Investigator will be agreed to in advance and be included in the contract Statement of Work or the Grant Terms of Award (notice of Grant Award). DAIDS reserves the right to submit an IND to the FDA even if there is no plan to conduct the study in the U.S.

Investigational New Drug or Biologic Product

If an investigational new drug or biologic has not received marketing approval from the FDA, then the sponsor must submit an IND pursuant to 21 CFR 312 to the FDA and allow the FDA 30 calendar days to review prior to initiating DAIDS sponsored and/or funded clinical trials.

Lawfully Marketed Drug and Biologic Products

If a drug or biologic product is already lawfully marketed in the United States, the IND regulations state that clinical investigation of a drug or biologic product is exempt from the requirements for an IND if **all** of the following apply:

- The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use, nor intended to be used to support any other significant change in the labeling for the drug or biologic product.
- The investigation is not intended to support a significant change in the advertising for a prescription drug or biologic product.
- The investigation does not involve a change in route of administration, dosage level, or patient population, or other factor that significantly increases the risks (or decreases the acceptability of risks) associated with use of the drug or biologic product.
- The investigation is conducted in compliance with the requirements for institutional review and informed consent regulations.

- The drug or biologic product may not be represented as safe or effective for the purposes for which it is under investigation, nor may it be commercially distributed or sold.

Generic Products

If a generic product is not lawfully marketed in the United States, then the Sponsor must submit an IND to the FDA.

If the generic product has received approval in the host country or from the WHO but has not received approval for marketing from the FDA, then the Sponsor must submit an IND.

FDA Consultation

If there is any question regarding the need to submit an IND to the FDA, RAB will consult with the FDA after conferring with pharmaceutical companies, the protocol team and/or PI and other DAIDS program staff.

Studies Outside the U.S.

For studies conducted outside of the U.S., the PI is responsible for submitting all the necessary documents to the host country regulatory authorities in accordance with local requirements. Documentation of all correspondence and approval from the host country regulatory authorities must be provided to the appropriate DAIDS program staff prior to study initiation in the host country.

7.0 REFERENCES

Code of Federal Regulations, Title 21, Part 312

http://www.access.gpo.gov/nara/cfr/waisidx_99/21cfr312_99.html

Center for Biologics Evaluation and Research

www.fda.gov/cber/

Center for Drug Evaluation and Research

www.fda.gov/cder/

8.0 INQUIRIES

Questions and comments regarding this policy may be directed to the OPCRO Policy Group at:

NIAIDOPCROPOLICYGROUP@mail.nih.gov

9.0 AVAILABILITY

This policy is available electronically at the following URL:
http://www3.niaid.nih.gov/research/resources/DAIDSClinRsrch/Default.htm

The signed original is maintained in the OPCRO policy office.

10.0 CHANGE SUMMARY

Version #	Date	Replaces	Date of Revision	Rationale for Revision/Retirement
1.0	14 JUL 06	N/A	N/A	N/A

11.0 APPENDICES

None.

12.0 APPROVAL

	Signature	Program/Branch	Date
Authorized By:	Richard Hafner, MD Director	Office for Policy in Clinical Research Operations	July 14, 2006